Remarks

As indicated in the Office Action, claims 1, 5, 7-13, 16-18, 20-22, 26, 28-34, 37, 38, and 40-46 are pending. Applicants wish to thank Examiner Angell for his courtesy on October 15, 2009, in discussing the restrictions set forth in the Office Action. In response to the Office Action, Applicants have amended the claims to clarify the present invention.

In the Office Action, the Examiner stated (a) restriction is required under 35 U.S.C. §121 and 35 U.S.C. §372 and (b) Applicant is required to elect a group of claims for prosecution between Groups I and XVI (*sic*, I-XVII, the Office Action identifies Group XII twice). The Office Action also provides Group I (claims 1, 11, 12, 20, and 21) of the claims is drawn to a method of inhibiting tumor angiogenesis comprising administering an effective amount of TSP-1 or a derivative thereof; Group II (claims 1, 11, 12, 20, and 21) is drawn to a method of inhibiting tumor angiogenesis comprising administering an effective amount of TSP-1 agonist or mimetic; Group III (claims 1, 9-12, 20, and 21) is drawn to a method of inhibiting tumor angiogenesis comprising administering an effective amount of an inhibitor of HGF/SF; Group IV (claims 1, 9-12, 20 and 21) is drawn to a method of inhibiting tumor angiogenesis comprising administering an effective amount of an inhibitor of Met (the HGF/SF receptor); Group V (claims 1, 5, 7, 8, 11, 12, 20 and 21) is drawn to a method of inhibiting tumor angiogenesis comprising administering an effective amount of an inhibitor of VEGF; Group VI (claims 1, 5, 7, 8, 11, 12, 20, and 21) is drawn to a method of inhibiting tumor angiogenesis comprising administering an effective amount of an inhibitor of the VEGF receptor; Group VII (claims 13, and 16-18) is drawn to a method of inhibiting tumor angiogenesis comprising administering an effective amount of an inhibitor of the MAPK pathway and an agent that inhibits upregulation of VEGF; Group VIII

(claims 13, 16-18) is drawn to a method of inhibiting tumor angiogenesis comprising administering an effective amount of an inhibitor of the MAPK pathway and an agent that inhibits down-regulation of TSP-1; Group IX (claims 22 and 32) is drawn to a composition comprising TSP-1 or a derivative thereof; Group X (claims 22 and 32) is drawn to a composition comprising a TSP-1 agonist/mimetic; Group XI (claims 22, 30, 31, 32, 43-46) is drawn to a composition comprising an inhibitor of HGF/SF; Group XII, first occurrence (claims 22, 30, 31, 32, and 43-46) is drawn to a composition comprising an inhibitor of Met (HGF/SF receptor); Group XII, second occurrence (claims 22, 26, 28, 29, 32, 33, and 43-46) is drawn to a composition comprising an inhibitor of VEGF; Group XIII (claims 22, 26, 28, 29, 32, 33, and 43-46) is drawn to a composition comprising an inhibitor of VEGF receptor; Group XIV (claims 34, and 37-42) is drawn to a composition comprising at least two inhibitors of the MAPK pathway and an agent that inhibits upregulation of VEGF; Group XV (claims 34, and 37-42) is drawn to a composition comprising at least two inhibitors of the MAPK pathway and an agent that inhibits upregulation of VEGF receptor; and Group XVI (claims 34, and 37-42) is drawn to a composition comprising at least two inhibitors of the MAPK pathway and an agent that inhibits down-regulation of TSP-1.

Applicants provisionally elect Group IX with traverse. Claims 22 and 32 encompass the invention. More specifically, as discussed during the October 15, 2009, telephone call with the Examiner, the invention is generally directed to a composition (or a method) that comprises (a) one or more of TSP-1, a TSP-1 derivative, a TSP-1 agonist, or a TSP-1 mimetic in combination with (b) one or more of an inhibitor of HGF/SF, Met, VEGF and/or the VEGF receptor. To the

extent that the claims may have been unclear, Applicants have amended the claims to further clarify that the invention is directed to the specified combination.

Further, the Office Action (at page 5) indicates that the invention does not make a contribution over the prior art WO 01/66114 (Office Action, p. 5). This reference discloses the combination of TSP and CPT-11. Because CPT-11 is an inhibitor or DNA topoisormerase I enzyme activity, Applicants respectfully contend that the composition and method of the present invention is novel over the combination of TSP and CPT-11 disclosed in WO 01/66114.

Further, the Office Action (page 6) indicates that Applicants are required to make species elections from each of three groups of species: (1) VEGF inhibitor or VEGF receptor and a single species thereof as listed in claims 5, 7, 8, 28, and 29; (2) HGF/SF inhibitor or Met inhibitor and a single species thereof as listed in claims 9, 10, 30, 31, and 32 and (3) a single MEK inhibitor as listed in claims 16, 17, 18, 37, and 38.

As to species group (1): Applicants elect a VEGF inhibitor; an anti-VEGF antibody; and an anti-VEGF monoclonal antibody termed Avastin®. Claims 1, 5, 7, 8, 12, 20-22, 26, 28, 29, 32- 34, and 43-46 cover the elected invention.

As to species group (2): Applicants elect a Met inhibitor; and an inhibitor of the kinase domain of Met. Claims 1, 9, 10, 22, 30, and 31 cover the elected invention.

As to species group (3): Applicants elect a small organic molecule. Claims 17, 38, and 42 cover the elected invention.

Conclusion

Applicants respectfully request entry of this Amendment and Response. The Examiner is invited to telephone Applicants' undersigned representative at (616) 942-6121 to discuss any outstanding issues.

All pending claims are believed to be in condition for allowance, and a Notice of Allowability is therefore earnestly solicited. If the Examining Attorney has any questions regarding this election, Applicants respectfully request that the Examining Attorney contact the undersigned at the telephone number indicated below or email the undersigned at dsiegel@priceheneveld.com.

Respectfully submitted,

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Date

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